

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Dean L. Engelhardt et al.)	
Serial No.	08/486,066)	Group Art Unit: 1812
Filed:	June 7, 1995)	Examiner: Not Yet Known
Title:	SUGAR MOIETY LABELED NUCLEOTIDES)	Prev. Exr: Gnan Wang, Ph.D. Prev. Group Art Unit: 1812

575 Fifth Avenue, 18th Floor
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Hon. Commissioner of Patents and Trademarks
Washington, D.C. 20231

**INFORMATION DISCLOSURE
STATEMENT UNDER 37 C.F.R. §§1.56 & 1.97-1.98**

Dear Sirs:

Pursuant to the provisions of 37 C.F.R. §§1.97-1.98, and in full compliance with their duty of disclosure under 37 C.F.R. §1.56, Applicants, through their attorney, are bringing the following one hundred and two (102) documents to the attention of the U.S. Patent and Trademark Office and the Examiner handling their above-identified application:

- JSB 1. Becker et al., "Irreversible Inhibition of Biotin Transport in Yeast by Biotinyl-p-nitrophenyl Ester," Proc. Nat'l. Acad. Sci. (USA) **68**:2604-2607 (1971)¹ [Exhibit 1];
- JSB 2. Halloran et al., "The Preparation of Nucleotide-protein Conjugates: Carbodiimides as Coupling Agents," J. Immunol. **96**:373-378 (1966)¹ [Exhibit 2];
- JSB 3. Manning et al., "A New Method of in situ Hybridization," Chromosoma **53**:107-117 (1975)¹ [Exhibit 3];
- JSB4. Kropinski et al., Gen. Virol. **6**:85 (1970)^{1,5} [Exhibit 4];

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EXPRESS MAIL CERTIFICATE	
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I hereby certify that this paper and the attachments herein are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington DC 20231	
<i>[Signature]</i> Ronald C. Fedus	SEPT 11, 1995 Date

- JSB5. Kropinski et al., "5-(4-Aminobutylaminomethyl) uracil, an Unusual Pyrimidine from the Deoxyribonucleic Acid of Bacteriophage ϕ W-14," Biochemistry, 12:151-157 (1973)¹ [Exhibit 5];
- JSB6. Bhat, Syn. Proc. in Nucleic Acid Chem., Vol. I., p. 521 (1968)^{1,5} [Exhibit 6];
- JSB 7. Torrence et al., "5-O-Alkylated Derivatives of 5-Hydroxy-2'-deoxyuridine as Potential Antiviral Agents. Anti-Herpes Activity of 5-Propynyloxy-2'-deoxyuridine," J. Med. Chem., 21:228-231 (1978)¹ [Exhibit 7];
- JSB8. Michelson, "Synthesis Of Nucleotide Anhydrides By Anion Exchange," Biochem. Biophys. Acta., 91:1-13 (1964)¹ [Exhibit 8];
- JSB 9. Cech et al. "A facile synthesis of 5-(perfluoroalkyl)-pyrimidines," Nucl. Acids Res., 2:2183-2192 (1979)¹ [Exhibit 9];
- JSB10. Schram et al., "Pyrrolopyrimidine Nucleosides VIII. Synthesis of Sanglivamycin Derivatives Possessing Exocyclic Heterocycles at C5," J. Carbohydrate. Nucleosides. Nucleotides, 1:39-54 (1974)¹ [Exhibit 10];
- JSB 11. Bleackley et al., "The preparation of 5-cyanouracil and 5-cyano-2'-deoxyuridine from the corresponding 5-iodo derivative and cuprous cyanide," Nucl. Acids Res., 2:683-690 (1975)¹ [Exhibit 11];
- JSB 12. Roberts et al., "Uridine and Cytidine Derivatives," J. Am. Chem. Soc. 74:668-669 (1952)¹ [Exhibit 12];
- JSB 13. Bauman et al., "Rapid and High Resolution Detection of in situ Hybridisation to Polytene Chromosomes Using Fluorochrome-labeled RNA," Chromosoma, 84:1-18 (1982)¹ [Exhibit 13];
- JSB 14. Bauman et al., "A new method for fluorescence microscopical localization of specific DNA sequences by in situ hybridization of fluorochrome-labelled RNA," Exp. Cell Res., 128:485-490 (1980)¹ [Exhibit 14];

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- JSB 15. Gerhard et al., "Localization of a Unique Gene by Direct Hybridization in situ," Proc. Natl. Acad. Sci. (USA), **78**:3755-3759 (1981)¹ [Exhibit 15];
- JSB 16. Miller, J., "Experiment 52, Assay of the lac Repressor by Binding to Operator," Experiments in Molecular Genetics, Cold Spring Harbor Laboratory pp. 367-370 (1972)¹ [Exhibit 16];
- JSB 17. Ueda et al., "Conversion of Uridine Nucleotides to the 6-Cyano Derivatives: Synthesis of Orotidylic Acid (Nucleosides and Nucleotides)," J. Carbohydr. Nucleosides, Nucleotides, **5**:261-271 (1978)¹ [Exhibit 17];
- JSB 18. Brunngraber et al., "Purification and Properties of a Nucleoside Phosphotransferase from Carrot," J. Biol. Chem., **242**:4834-4840 (1967)¹ [Exhibit 18];
- JSB 19. Wilchek et al., "Modification of the Carboxyl Groups of Ribonuclease by Attachment of Glycine or Alanylglycine," Biochemistry, **6**:247-252 (1967)¹ [Exhibit 19];
- JSB 20. Vogt, "Purification and Properties of S₁ Nuclease from *Aspergillus*," Methods in Enzymology, **65**:248-255 (1980)¹ [Exhibit 20];
- JSB 21. Ward et al., U.S. Patent No. 4,711,955, Issued December 8, 1987 (the application of which is a continuation of U.S. Patent Application Serial No. 255,223, filed April 17, 1981 and abandoned¹) [Exhibit 21];
- JSB 22. Monod et al., "On the Nature of Allosteric Transitions: A Plausible Model," J. Mol. Biol., **12**:88-118 (1965)¹ [Exhibit 22];
- JSB 23. Pastan et al., "Cyclic Adenosine Monophosphate in Bacteria," Science, **169**:339-344 (1969)¹ [Exhibit 23];
- JSB 24. Gilbert et al., "The Nucleotide Sequence of the lac Operator," Proc. Natl. Acad. Sci. (USA), **70**:3581-3584 (1973)¹ [Exhibit 24];
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- JSB25. Pardee, "Membrane Transport Proteins," Science, 162:632-637 (1968)¹ [Exhibit 25];
- JSB 26. Hazelbaur et al., "Role of the Galactose Binding Protein in Chemotaxis of Escherichia coli toward Galactose," Nature New Bio., 230:101-104 (1971)¹ [Exhibit 26];
- JSB 27. Caruthers, Second Annual Congress for Recombinant DNA Research, Los Angeles, CA (1982)^{1, 5} [Exhibit 27];
- JSB 28. Stavrianopoulos, U.S. Patent No. 4,707,440, issued November 17, 1987^{2, 7} [Exhibit 28];
- JSB 29. Robins et al., U.S. Patent No. 4,038,480, issued July 26, 1977^{2, 7, 8} [Exhibit 29];
- JSB30. Carrico et al., U.S. Patent No. 4,213,893, issued July 22, 1980^{2, 7, 8, 23} [Exhibit 30];
- JSB31. Carrico et al., U.S. Patent No. 4,255,566, issued March 10, 1981^{2, 4, 7, 8, 21, 23} [Exhibit 31];
- JSB 32. Gohlke et al., U.S. Patent No. 4,378,458, issued March 29, 1983^{2, 7, 8, 19} [Exhibit 32];
- JSB33. Bückmann, U.S. Patent No. 4,443,594, issued April 17, 1984^{2, 7, 8} [Exhibit 33];
- JSB 34. Japan Patent No. 53-133283 (Agency Ind. Sci.) (November 1978)^{2, 8, 28} [Exhibit 34];
- JSB 35. Imahori et al., U.K. Patent Application No. GB 2 036 029 A, published June 25, 1980^{2, 8} [Exhibit 35];
- JSB 36. Japan Patent No. 57-11999 (Chugai Pharm.) (January 1982)^{2, 8, 28} [Exhibit 36];

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- JSB 37. Japan Patent No. 60-96610 (Agency Ind. Sci.) (May 1985)^{2,6,*} [Exhibit 37];
- JSB 38. Ward et al., European Patent No. 0 063 879 B1, granted November 23, 1989^{2,4},
8, 14, 15, 16, 18, 19 [Exhibit 38];
- JSB 39. Carrico et al., U.K. Patent Application No. GB 2 040 943 A, published
September 3, 1980^{2,4,21} [Exhibit 39];
- JSB 40. Langer et al., "Enzymatic synthesis of biotin-labeled polynucleotides: Novel
nucleic acid affinity probes," Proc. Natl. Acad. Sci. (USA), 78:6633-6637
(1981)^{2,4,9,18,22} [Exhibit 40];
- JSB⁴¹. Nishimura et al., "Synthetic Nucleosides and Nucleotides. XV. 1) 5-
Dimethylamino-2-oxidoisoquinolin-1-yl Diazomethane: A Novel Water-Soluble
Fluorescent Labelling Agent for Nucleotides," Chem. Pharm. Bull., 28:1695-1703
(1980)^{2,4} [Exhibit 41];
- JSB 42. Kwah et al., "Myocardial Infarct Imaging of Antibodies to Canine Cardiac
Myosin with Indium-111-Diethylenetriamine Pentaacetic Acid," Science 209:295-
297 (1980)³ [Exhibit 42];
- JSB 43. Benovic et al., U.S. Patent No. 4,460,772, issued July 17, 1984⁵
[Exhibit 43];
- JSB 44. Torrence et al., "Interferon Inducers: General Survey and Classification,"
Methods in Enzymology, Vol. 78, Interferons, Part A, pp. 291-299 (Pestka,
Edu.), Academic Press, New York, 1981¹⁰ [Exhibit 44];
- JSB 45. Hamden, U.S. Patent No. 3,931,397, issued January 6, 1976¹¹ [Exhibit 45] ;
- JSB 46. Lampson et al., U.S. Patent No. 4,124,702, issued November 7, 1978¹¹ [Exhibit
46] ;
- JSB⁴⁷. Arimura et al., U.S. Patent No. 4,313,938, issued February 2, 1982¹¹ [Exhibit
47];
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- JSB 48. Ward et al., U.S. Patent No. 4,711,955, issued December 8, 1987^{9, 12, 15, 16, 22, 24}
[Exhibit 48][NOTE THAT ONLY THE FIRST PAGE OF THIS PATENT IS
SUBMITTED AS EXHIBIT 48 HERewith; A COMPLETE COPY OF THIS
PATENT WAS PREVIOUSLY SUBMITTED HERewith AS EXHIBIT 21
ABOVE];
- JSB 49. Falkow et al., U.S. Patent No. 4,358,535, issued November 9, 1982^{12, 14, 15, 16, 17,}
²⁴ [Exhibit 49];
- JSB 50. Engelhardt et al., U.S. Patent No. 5,260,433, issued November 9, 1993¹³
[Exhibit 50];
- JSB 51. Kourilsky et al., United Kingdom Patent Application No. GB 2 019 408 A,
published October 31, 1979^{14, 16} [Exhibit 51];
- JSB 52. Kourilsky et al., U.S. Patent No. 4,581,333, issued April 8, 1986¹⁶ [Exhibit 52];
- JSB 53. Siebenlist et al., "Contacts between Escherichia coli RNA polymerase and an
early promoter of phage T7," Proc. Natl. Acad. Sci. (USA), 77:122-126, January
1980¹⁷ [Exhibit 53];
- JSB 54. Maxam et al., "A New Method for Sequencing DNA," Proc. Natl. Acad. Sci.
(USA), 74:560-564, 1977¹⁷ [Exhibit 54];
- JSB 55. Heggeness et al., "Avidin Binds To Condensed Chromatin," Stain Technol.
52:165-169 (1977)¹⁸ [Exhibit 55];
- JSB 56. Heggeness et al., "Use of the Avidin-Biotin Complex For the Localization of
Actin and Myosin with Fluorescence Microscopy," J. Cell Biol. 73:783-788
(1977)¹⁸ [Exhibit 56];
- JSB 57. Bayer et al., "The Use of the Avidin-Biotin Complex as a Tool in Molecular
Biology," Methods of Biochem Analysis 26:1-45 (1980)¹⁸ [Exhibit 57];

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- JSB 58. Hoffman et al., "Iminobiotin affinity columns and their application to retrieval of streptavidin," Proc. Natl. Acad. Sci. 77 :4666-4668 (1980)¹⁸ [Exhibit 58];
- JSB 59. Pardue et al., "Nucleic Acid Hybridization to the DNA of Cytological Preparations," Methods in Cell Biol. 10:1-16 (1975)¹⁸ [Exhibit 59];
- JSB 60. Bergstrom et al., "C-5 Substituted Pyrimidine Nucleosides. 2. Synthesis via Olefin Coupling to Organopalladium Intermediates Derived from Uridine and 2'-Deoxyuridine," JACS 100:8106-8112 (1978)¹⁸ [Exhibit 60];
- JSB 61. Bigge et al., "Palladium-Catalyzed Coupling Reactions of Uracil Nucleosides and Nucleotides," JACS 102:2033-2038 (1979)¹⁸ [Exhibit 61];
- JSB 62. Rigby et al., "Labeling Deoxyribonucleic Acid to High Specific Activity In Vitro by Nick Translation with DNA Polymerase I," J. Mol. Biol. 113:237-251 (1977)¹⁸ [Exhibit 62];
- JSB 63. Bourguignon et al., "DNA of Minute Virus of Mice: Self-Priming, Nonpermuted Single-Stranded Genome with a 5'-Terminal Hairpin Duplex," J. Virol. 20:290-306 (1976)¹⁸ [Exhibit 63];
- JSB 64. Miller et al., "A general method for permeabilizing mono-layer and suspension cultured animal cells," Exp. Cell Res. 120:421-425 (1979)¹⁸ [Exhibit 64];
- JSB 65. Miyoshi et al., U.S. Patent No. 4,605,735, issued August 12, 1986¹⁹ [Exhibit 65];
- JSB 66. Japan Patent No. 60-169495, issued September 1985^{19, 26} [Exhibit 66];
- JSB 67. Helene et al., European Patent Application No. 0 169 787 A1, published January 29, 1986^{19, 26} [Exhibit 67];
- JSB 68. Klevan et al., PCT Patent Application No. WO 86/02929, published May 22, 1986¹⁹ [Exhibit 68];
- JSB 69. Japan Patent No. 57-42632, issued March 1986^{19, 26} [Exhibit 69];
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JSB 70. Japan Patent 61-103824, issued May 1986^{19, 20} [Exhibit 70];

JSB71. Suhadolnik et al., U.S. Patent No. 9,708,935, issued November 24, 1987²⁰
[Exhibit 71];

JSB 72. Rapaport, U.S. Patent No. 4,880,918, issued November 14, 1989²⁰ [Exhibit 72];

JSB 73. Klevan et al., U.S. Patent No. 4,828,979, issued May 9, 1989²⁵ [Exhibit 73];

JSB74. Musso et al., U.S. Patent No. 4,833,251, issued May 23, 1989²⁵ [Exhibit 74];

JSB 75. Carrico et al., European Patent No. 0 027 631 B1, granted May 5, 1982²⁵
[Exhibit 75];

JSB 76. Urdea et al., European Patent Application No. 0 225 807 A2, published June
16, 1987²⁵ [Exhibit 76];

JSB 77. Schulman et al., "Attachment of protein affinity-labeling reagents of variable
length and amino acid specificity to E. coli tRNA^{Met}," Nuc. Acid Res. 9:1203-
1217; (1981)²⁵ [Exhibit 77];

JSB78. Langer, et al., "Enzymatic synthesis of biotin-labeled polynucleotides: Novel
nucleic acid affinity probes," Chemical Abstracts, Vol. 96, No. 7, February 15,
1982, pg. 207, Abstract No. 47771z²¹ [Exhibit 78];

JSB 79. Clechet, P. et al., "Trace analysis of barium in water by means of cation resin-
loaded paper and x-ray fluorescence analysis," Chemical Abstracts, Vol. 94, No.
25, June 22, 1981, pg. 366, Abstract No. 214298t⁴
[Exhibit 79];

JSB 80. Duke et al., "Conformational change accompanying modification of myosin
ATPase," Chemical Abstracts, Vol. 66, No. 9, February 27, 1967, pg. 3326,
Abstract No. 35045h⁴ [Exhibit 80];

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- JSB 81. Duke et al., "Conformational change accompanying modification of myosin ATPase," Biochem. Biophys. Acta, 126:600-603 (1966)⁴ [Exhibit 81];
- JSB 82. Secrist, III et al., U.S. Patent No. 3,960,840, issued June 1, 1976^{4,21} [Exhibit 82];
- JSB 83. Boguslaski et al., U.S. Patent No. 4,230,797, issued October 28, 1980^{4,21} [Exhibit 83];
- JSB 84. Kathawala et al., "Darstellung von Desoxy-oligonucleotiden Mit 2'.3'-[2.4-Dimethoxy-benzyliden]-uridin als Phosphat-Schutzgruppe," Liebigs Ann. Chem., 712:195-200 (1968)^{4,27} [Exhibit 84];
- JSB 85. Trouet et al., "Targeting of antitumor and antiprotozoal drugs by covalent linkage to protein carriers," Chemical Abstracts, Vol. 98, No. 9, February 28, 1983, pg. 334-335, Abstract No. 77997m⁴ [Exhibit 85];
- JSB 86. Trouet et al., "Targeting of antitumor and antiprotozoal drugs by covalent linkage to protein carriers," NATO Adv. Study Inst. of Targeting of Drugs, Series A, Life Sciences, 47:19-30, Plenum Press, New York (1981)⁴, [Exhibit 86];
- JSB 87. Kourilsky et al., PCT Application No. WO 83/02276, published July 7, 1983^{4,21} [Exhibit 87];
- JSB 88. Kourilsky et al., PCT Application No. WO 83/02277, published July 7, 1983^{4,21} [Exhibit 88];
- JSB 89. Angerer et al., "An Electron Microscope Study of the Relative Positions of the 4S and Ribosomal RNA Genes In HeLa Cell Mitochondrial DNA," Cell 9:81-90 (1976)⁴ [Exhibit 89];
- JSB 90. Scherberg, U.S. Patent No. 4,260,737, issued April 7, 1981⁴ [Exhibit 90];

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- JSB 91. Mackey et al., "Preparation and Characterization of Highly Radioactive in Vitro Labeled Adenovirus DNA and DNA Restriction Fragments," Biochemistry, 16:4478-4482 (1977)⁴ [Exhibit 91];
- JSB 92. Zhenodarova et al., "Spin-labeled Derivatives of Oligoribonucleotides as Spin Probes for Studying the Mechanism of the Effect of Enzymes," Chemical Abstracts, Vol. 91, 1979, pg. 303, Abstract No. 85951n⁴ [Exhibit 92];
- JSB 93. Institute of Biophysics et al., Soviet Union Patent Application A 659 573, April 30, 1979^{4,6} [Exhibit 93];
- JSB 94. Crea, U.S. Patent No. 4,310,662, issued January 12, 1982⁴ [Exhibit 94];
- JSB 95. Salam et al., "Synthesis of Nucleoside 5'-(β -D-Glucopyranosyl Monophosphates) by the Sugar Ortho Ester Route," Carbohydrate Research, 102:139-146 (1982)⁴ [Exhibit 95];
- JSB 96. Salam et al., "Synthesis of Acetylated α - and β -L-Fucosyl Esters of Nucleoside 5'-Monophosphates by the Orthoester Route," Nucleosides & Nucleotides, 1:155-161 (1982)⁴ [Exhibit 96];
- JSB 97. Gohlke et al., European Patent Application No. O 061 762 A2, published October 6, 1982⁴ [Exhibit 97];
- JSB 98. Kang et al., European Patent Application No. O 061 760 A1, published October 6, 1982⁴ [Exhibit 98];
- JSB 99. Kang, European Patent Application No. O 061 761 A1, published October 6, 1982⁴ [Exhibit 99];
- JSB 100. Sela et al., German Patent Application No. DE-A-25-07-901, published September 10, 1970^{4,26} [Exhibit 100];
- JSB 101. Theurer, German Patent Application No. DE-A-18-14-134, published January 28, 1971^{4,26} [Exhibit 101]; and

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JSB 102. Theurer, German Patent Application No. DE-A-16-17-886, published September 2, 1976^{4, 28} [Exhibit 102].

Of the one hundred and two (102) above-submitted documents, twenty-seven (27) documents (Exhibits 1-27) were cited in the instant specification; fifty-five (55) documents (Exhibits 28-78, 82-83 and 87-88) were cited or made of record in the prosecution of related applications; and thirty (30) documents (Exhibits 31, 38-41 and 78-102) were cited by the European Patent Office in the prosecution of the six (6) corresponding European applications, namely application numbers: 83106112.2 which issued as European Patent No. 0 097 373 B1, 0 285 057 A2, 0 285 950 A3, 0 302 175 A3, 0 286 898 A3, 0 285 058 A3, published October 10, 1992, October 5, 1988, October 12, 1988, February 8, 1989, October 19, 1988 and October 5, 1988, respectively.

A completed Form PTO-1449 listing the above-submitted documents is also attached hereto as Exhibit 103.

By this voluntary citation of art, Applicants and their attorney are requesting that the documents be made of record in the instant application.

The above citation of references is not a representation that these documents constitute a complete or exhaustive listing, nor that the above listing necessarily includes the closest or most relevant references, nor are these documents necessarily a complete listing of all references known to Applicants or their attorney. It is simply a voluntary citation of references made in good faith, which is not intended to serve in any way as a substitute for the Examiner's own search.

In view of the general and specific features described and claimed in the present application, Applicants respectfully submit that the present invention is neither suggested nor disclosed by the documents referred to above and is thus patentably distinct thereover.

Applicants do not believe, and do not submit, by the citation of these references, that these references, either by themselves or in combination with other
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